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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/080,428	02/22/2002	Virginia L. Price	3141-A	8280

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EXAMINER	
MCKELVEY, TERRY ALAN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/080,428	PRICE ET AL.	
	Examiner	Art Unit	
	Terry A. McKelvey	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-34* is/are pending in the application.

4a) Of the above claim(s) *14-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/6/03; 1/28/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5-0-0

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, species p65, CMV promoter, antibody, and CHO cells, claims 1 and 4-13 in the reply filed on 9/22/04 is acknowledged.

Claims 14-34 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/22/04.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 4-9, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilman et al (U.S. Patent No. 6,306,649 B1) in view of La Rosa et al.

Gilman et al teach improved methods for achieving high-level expression of a target gene in genetically engineered cells comprising introducing into a cell a transcription factor construct containing a first heterologous DNA sequence which expresses a transcription factor capable of activating transcription of a gene linked to a control sequence responsive to the transcription factor and a target gene construct containing a second heterologous DNA sequence comprising a target gene operably linked to the transcription control sequence (column 1). The transcription factor may be a naturally occurring protein, especially if it is heterologous to the cell type to be engineered (column 5). While the resultant

increases in activation potency are dramatic, p65-based transcription factors possess additional and unexpected characteristics. For instance, unlike VP16, our p65-based activators do not appear to be toxic to the engineered cells (column 11). A variety of genes can be employed as the target gene, including genes that encode a secreted therapeutic protein, such as antibodies (columns 16 and 23). The promoter used to express the transcription factor include those from a variety of sources, including heterologous promoter regions from hCMV and CMV (column 17). The constructs encoding the transcription factor and the target gene construct can be introduced into cells in association with one or more markers to allow selection (column 20). The invention is particularly useful for the engineering of animal cells, such as mammalian cells (columns 19-20).

Gilman et al do not specifically teach the use of p65 itself as the transcription factor in the method, or p65 and another NF-kappa-B transcription factor.

La Rossa et al teach that classical NF-kappa-B (p65/p50) is a potent transcriptional activator of the c-myc promoter, and that co-transfection of either p65 alone or p65 in combination with p50 mediated significant induction (abstract).

Transfection of p65 alone resulted in stimulation of expression to a lesser extent (page 1040, column 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the expression method taught by Gilman et al by using as the transcription factor to be expressed in the method p65 alone or p65 and p50 (and using the c-myc promoter as the promoter that responds to the transcription factor) because Gilman et al teach that it is within the ordinary skill in the art to use a naturally occurring transcription factor in the method and transcription factors based upon p65 and La Rossa et al teach that it is within the ordinary skill in the art to express p65 or p65 and p50 to increase expression from the c-myc promoter.

One would have been motivated to do so for the expected benefit of increasing expression from the c-myc promoter as taught by La Rossa et al applied to increasing expression of secreted proteins such as antibodies, which increased expression is not toxic to the cell because it is based upon p65, as taught by Gilman et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 4-11, and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilman et al and La Rossa et al as applied to claims 1, 4-9, and 13 above, and further in view of Kushner et al (U.S. Patent No. 5,089,397).

Gilman et al and La Rossa et al are described above and applied as before.

These two references do not specifically teach the use of CHO cells or host cells that is adapted to protein-free medium.

Kushner et al teach that CHO cells can be maintained in protein-free medium, are fast growing, well characterized, free of recognizable dangers, and are thus ideal hosts for recombinant protein production (column 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use as host cells in the method made obvious from the combined teachings of Gilman et al and La Rossa et al, CHO cells, adapted to protein-free medium because Gilman et al teach that it is within the ordinary skill in the art to use mammalian cells for the expression method and Kushner et al teach that it is within the ordinary skill in the art to use CHO cells and protein-free medium for recombinant protein expression.

One would have been motivated to do so for the expected benefit of using CHO cells in the expression method that are fast growing, well characterized, capable of growing in protein-free medium, free of recognizable dangers, and are thus ideal hosts for recombinant protein production as taught by Kushner et al. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 4-9, and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gilman et al and La Rossa et al as applied to claims 1, 4-9, and 13 above, and further in view of Levkau et al (applicant reference C8).

Gilman et al and La Rossa et al are described above and applied as before.

These two references do not specifically teach the use of caspase-resistant mutant as the p65 transcription factor to be used in the method.

Levkau et al teach a caspase-resistant mutant of p65 (abstract). This p65 mutant is uncleavable and it protects cells from apoptosis more than wild type p65 (page 230-231). This reference also teaches that cleaved p65 is a dominant-

negative inhibitor of transcription, suppressing expression from p65-responsive promoters (page 231, second paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the caspase-resistant p65 as the p65 transcription factor used in the methods made obvious from the combined teachings of Gilman et al and La Rossa et al because Gilman et al and La Rossa make obvious that it is within the ordinary skill in the art to use p65 as the transcription factor in the expression method made obvious from their teachings, and that p65-based transcription factor increased expression is not toxic to cells and Levkau et al teaches that the caspase-resistant p65 is uncleavable, and that cleaved p65 is a dominant-negative inhibitor of transcription.

One would have been motivated to do so for the expected benefit of reducing cleavage of p65 in the expression system made obvious from the combined teachings of the cited references, resulting in less inhibition of expression from p65-responsive promoters, and thus increasing expression from such promoters which include the c-myc promoter. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary,

there would have been a reasonable expectation of success to result in the claimed invention.

Conclusion

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily

from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (571) 272-0775. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be

responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached at (571) 272-0781.

Terry A. McKelvey, Ph.D.
Primary Examiner
Art Unit 1636

August 8, 2005